UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,719	08/22/2000	Margret Hoehe	101195-2	8381

7590 06/02/2004

Bruce S Londa
Norris McLaughlin & Marcus
220 EAST 42 nd STREET 30th FLOOR
New York, NY 10017

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,719	HOEHE ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *2,4-8,22,24-30,32,33,37,38,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3,9-21,31,34-36,39,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/15/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Claims 2, 4-8, 22, 24-30 and 32, 33, 37, 38, 40, 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 10/09/93.

Applicant argues that no reasons were given as to why the amendment of 6/6/02 and arguments necessitated a new restriction requirement. This argument has been fully considered but not deemed persuasive. As argued by Applicant at page 5 of Applicant's 9/9/02 response, the amendment made the prior restriction requirement improper.

Applicant argues that 37 CFR 1.475(d) does not apply to multiple related products. This argument has been fully considered but not deemed persuasive; Applicant is referred to the text of the rule and also to 37 CFR 1.475(e), below:

§ 1.475 Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage.

(d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).
(e) The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Applicant argues that page two of the Unity of Invention Practice Guidelines indicates that variants of a single gene are not viewed as distinct inventions. This argument has been fully

considered but not deemed persuasive. Nowhere on page 2 does it state or suggest that variants of a single gene are not viewed as distinct inventions. The examiner can find no basis for Applicant's arguments in the remaining pages referred to by Applicant.

Applicant expressed confusion regarding the statement that there is no method of making the polynucleotide. This was simply a statement that no claim to that effect was in the Group.

Applicant request that the examiner point-out wherein the response did Applicant concede that each allele is a non-obvious variant of the others. At page 6 of the 9/9/02 response Applicant asserts the following:

"Applicants respectfully point out that the sequence variants at nucleic acid positions 1633, 1666 and 2078 (attributed to the Turki, et al) have been deleted from amended independent claims 1 and 9.

Thus, because the amended claims would overcome an obviousness rejection over Turki et al., the amended claims clearly possess a linking special technical feature."

Here, Applicant has removed one variant from the claim, and indicates that the remaining variants would not be obvious over the variant. These statements were taken to mean that the variants are not obvious over each other, and are agreed with by the examiner.

Applicant's analysis and arguments regarding Markush practice have been fully considered but are not persuasive. While Applicant is free to structure claims in a variety of formats, PCT Rules provide for examination of first named product (singular), method of making and method of using, 37 CFR 1.475. Further, the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard

to whether the inventions are claimed in separate claims or as alternatives within a single claim 37 CFR 1.475(e). As set forth previously, the technical feature of generic claims 1 and 9, i.e., that alleles of an adrenergic receptor are associated with diseases, is not a special technical feature, under PCT Rule 13.2, because this technical feature was known in the prior art, e.g. TURKI et al.

Applicant disagrees with the assertion that the mutants are directed to an indecipherable number of disease, however Applicant has not provided any reasons as to challenge the examiner's assertion. There do not appear to be many known diseases that couldn't reasonably be encompassed by the categories recited in, e.g., claim 18.

Applicant argues that a common structural feature is shared by all the variants, e.g. 99.5% structural identity. This argument has been fully considered but not deemed persuasive. This feature can not be as special technical feature under PCT Rule 13.2, because this technical feature was known in the prior art, e.g. TURKI et al.

Applicant's arguments have been fully and carefully considered, however, the restriction requirement is deemed to be proper and is maintained and made FINAL. Thus, Applicant is reminded that the claims will be examined only to the extent that they read on the elected species of allele, 1541T;1633A;1666C, and to the species of hypertension, as elected in the 9/9/02 response.

Additional Advisory Information:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product *claim is subsequently found allowable*,

withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01

Priority

If applicant desires priority under 35 U.S.C. 119 or 365(c) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time

period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3, 31, 34, 35, 36, 39, 42and 43 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read on the DNA that would be present in a human being and are thus not patentable under 35 USC 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 9, 10-21, 23, 31, 34, 35, 36, 42, 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require substitutions in particular positions in a polynucleotide without reference to a specific sequence or sequence identifier, and are thus indefinite because the artisan could not reasonably know which positions the claims are referring to.

Claims 1, 3 and 42 claim "sequence of a human β2-adernergic receptor gene", however it is unclear what this statement refers to, i.e. a sequence of what?, DNA or symbols or letters?

Claims 10-17 and 31 require that the positions be "genotypified" or that the method involves "genotypifying". These words do not appear to be used in the art, and nor does the specification define them, thus the artisan could not know what limitations are placed on the claims by the presence of these terms.

Claims 34, 35, 36, 39, 43 require "a variant"; this renders the claims indefinite because the term is a relevant term and the specification does not set forth the degree to which the claimed subject matter is allowed to vary; thus the artisan could not reasonably be sure that he or she was in possession of what is claimed.

Claim 31 provides for the use of the sequence variants, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is

intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 31 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Similarly, claims 9-21 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims lack a step or steps to follow which lead back to and accomplish the goal, set forth in the preamble, of determining the disposition of disease.

Regarding claims 18 and 21 the phrases "such as" or "e.g." or "diseases including" render the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Further Claim18 recites "determining a disposition to high blood pressure and deviations of the blood pressure from the standard and other cardiovascular diseases"; the examiner does not understand what this means.

Further, claims 18 and 23 present a bewildering array disparate disorders which are referred to specifically only by example or only generally, e.g. "cardiovascular disease" and "neuropsychiatric diseases" and "diseases of the autonomic nervous system" and "metabolic diseases", these broad categories due not place limitations on the claims such that an artisan would reasonably know whether or not a particular disease was within or outside of the scope of what is being claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-12, 23, 34, 35, 36, 42, 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining the disposition to hypertension by detecting the presence of the 1541T, 1568T, 1633A, 1666C allele of SEQ ID NO: 1 and determining the disposition to asthma by detecting the presence of the 1633 allele (as taught by Turki et al.), does not reasonably provide enablement for methods of determining the disposition to any other diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth above, the claims encompass a bewildering array disparate disorders which are referred to specifically only by example or only generally, e.g. "cardiovascular disease" and "neuropsychiatric diseases" and "diseases of the autonomic nervous system" and "metabolic diseases", yet the specification has provided evidence only involving hypertension, i.e. page seven. Further, TURKI et al., J. Clin. Invs. 95(1635-1641)1995 disclose bases changes at positions 1633, 1666, and 2078, of the human beta2 adrenergic receptor gene and further indicate that an allele harboring the 1633 mutation is correlated with nocturnal asthma (see page 1637). The specification however, simply speculates that the these mutations would underlie a host of other, seemingly disparate disease states. If this were indeed true, then one wonders how these

diseases would have escaped the notice of TURKI et al. when they conducted their clinical investigations. Regardless, the specification has simply presented an invitation to the artisan to begin an essentially random trial and error plan of extensive experimentation, of the type conducted by TURKI, wherein patients with any disorder are tested for these mutations in the hope of finding a correlation. "Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech, Inc. v. Novo Nordisk Inc., 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997).

The claims are in essence single means claims because the specification offers only a single means, i.e. detecting the presence of a particular allele, 1541T, 1568T, 1633A, 1666C and correlating it with a single disorder, i.e. hypertension, yet the claims encompass a tremendous diversity of alleles that are required to be used to determine the disposition to an immensely vast genus of disparate disease states.

In *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a).

Further, the specification has failed to teach how to use polynucleotides of claims 1, 34, 35, 36, 42, 43 without undue experimentation. The specification fails to assert that these alleles

are correlated with any particular disorder of phenotype (with the exception of the 1541T, 1568T, 1633A, 1666C allele), thus the invitation to find such, as discussed above, is unduly burdensome.

Therefore, due to the large amount of experimentation required to find other correlations between the myriad allele types presented in the specification and the myriad of disease types speculated by the specification to correlate with the alleles, if such correlations can be found, the complex nature of the autonomic nervous system, the lack of particular information provided by the specification, e.g. allele X correlates with disease Y, the apparent contradictory state of the art as exemplified by TURKI et al., who conducted a clinical trial with patients having alleles recited in the specification yet failed to notice other diseases associated with the alleles, the breadth of the claims which encompass almost every conceivable metabolic disease, it would require undue experimentation by one skilled in the art to make and use the invention commensurate in scope to that which is claimed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D., can be reached at (571) 272-0887.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

May 28, 2004

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

LORRAINE SPECTOR
PRIMARY EXAMINER

May 28, 2004